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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,686	07/10/2006	David Edmund Wright	MKC-001	2900

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EXAMINER	
MUI, CHRISTINE T	
ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,686	WRIGHT, DAVID EDMUND	
	Examiner	Art Unit	
	CHRISTINE T. MUI	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,8,9,11,12,14-20,22,23,25-27,32,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8,9,11,12,14-20,22,23,25-27,32,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01 March 2010 has been entered.

Response to Arguments

2. Applicant's arguments, see REMARKS/RCE, filed 01 March 2010, with respect to claim 1 have been fully considered and are persuasive. The objection of claim 1 has been withdrawn.

Applicant's arguments filed 01 March 2010 have been fully considered but they are not persuasive.

Although Davies discloses only one biomarker measured at two different stages and Nicholls measures two more biomarkers at different stages of pregnancy, it would have been obvious to one having ordinary skill in the art at the time the invention was made to measure more than one biomarker in Davies to verify data compared to other women or to modify Nicholls so that there is an individual value for each marker defining each marker and basing conclusions on one specific parameter and since the court held

that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. *In re Harza*, 274 F.2d 669, 124 USPQ 378 (CCPA 1960). Furthermore, since Nicholls already measures two or more parameters and obtained values and created a single value, it would be less work during analysis if one was to just keep the individual values and not create a single value for two markers. Omitting the last step would create less analytical work after biomarker parameters are obtained.

Claim Rejections - 35 USC § 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-4, 6, 8, 9, 11, 12, 14-20, 22, 23, 25-27, 40, and 41 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The methods of the instant claims must meet a specialized, limited meaning to qualify as a patent-eligible process claim. The test is whether the claimed method is (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing. A machine is a "'concrete thing, consisting of parts, or of certain devices and combination of devices.' This 'includes every mechanical device or combination of mechanical powers and devices to perform some function and produce a certain effect or result. In re Nuijten, 500 F.3d 1346 (Fed. Cir. 2007). The Court stated in Bilski, "[p]urported transformations or manipulations simply of public or private legal obligations or relationships, business risks, or other such abstractions cannot meet the

test because they are not physical objects or substances, and they are not representative of physical objects or substances." 545 F.3d at 963.

Under current examination instructions, for data, mathematical manipulations per se has not been deemed to be a transformation. Furthermore, the method as claimed by the Applicant does not tie the test to a particular machine or apparatus. The method is just steps of manipulating and correlating data.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 14, 6, 8, 9, 11, 12, 14-20, 22, 23, 25-27, 32, 40 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 800 085 to Davies (submitted on the Information Disclosure Statement on 18 August 2006; herein referred 'Davies') and

further in view of WO 99/56132 to Nicholls et al (submitted on the Information Disclosure Statement on 18 August 2006; here referred 'Nicholls').

6. Regarding claim 1-3, 6, 8, 11, 12, 14-20, 22, 23, 25-27 and 32, the reference Davies discloses a method for antenatal screening for an abnormality in a fetus of a woman. The screening is determined using a bodily fluid, the fluid containing a marker at which at one stage of a gestation (stage A) and another stage of gestation (stage B). Stage A is the mean or median level of the marker differs by less than 20% between pregnancies which are affected and unaffected by the abnormality and Stage B marker differs by more than 50% between affected and unaffected pregnancies and a computer is provided for the means for comparing the measurements of the levels with each other and to sets of reference data to determine fetal abnormalities characterized in that the computer is capable of comparing concentrations. There is at least 3 weeks between Stage A and Stage B. The concentrations of the marker for an individual woman are made at Stage A and Stage B and are compared and a normalized concentration is determined and compared with similarly determined normalized concentrations. The serum marker that is identified in the samples are intact hCG or the free alpha or beta subunits of hCG as well as AFT, PAPP-A, dimeric inhibin (inhibin A) and Schwangerschaft protein (Pregnancy specific X-glycoprotein 1, SP1). In determining the likelihood of a chromosomal abnormality it is know that some markers are lower in concentration at particular stages, for example PAPP-A are known to be lower in the first trimester where the fetus has Down Syndrome, yet show no difference in the second trimester of pregnancy. The measurements are carried out and analyzed using

the method of invention on samples taken during an appropriate period of pregnancy. The measurements are taken in the first and second trimesters and often in the period between the beginning of the eighth week and the end of the second trimester. The concentrations of most maternal serum markers change during pregnancy as a result of changes in the size and maturity of the fetus or placenta and in order to enable valid comparisons between the concentrations at different stages of pregnancy, they must be normalized by dividing the actual value by the median value found in the unaffected population of pregnant women at that gestational age (the Multiple of the Median or MoM). The median is used to avoid any undue influence of outlying values. The serum value for the individual serum marker is divided by the normalized expected median value found in women with unaffected pregnancies at the same gestation age to derive the multiple of the median (MoM). The probability that the (MoM) values for the markers belongs to the multivariate distribution of values found in unaffected pregnancies is calculated. The same calculation is performed by reference to the probability that the individual combination of values forms part of the multivariate distribution found in abnormal pregnancies. The ratio of the probabilities is termed the likelihood ratio that indicates the likelihood that an individual woman has an affected pregnancy or not. The degree of separation between the multivariate distributions for affected and unaffected pregnancies changes with gestational age, i.e. there is a continuous change in the manner of calculating probability depending on the gestational age, and this change can be accounted for by an algorithm used in the calculation.

7. Davies does not specifically calculate the correlation between the two different stages, Stage A and Stage B; first trimester and second trimester, Davies does disclose that as seen in Figure 1, the median hCG concentration was determined at different weeks of gestation and the correlation is implied since both high values at stages or low values at stages is an indication of the risk for fetal Down Syndrome on account of the hCG concentration (see page 3, lines 1-55, page 4, lines 1-6, 40-56, Figure 1). It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the calculation between all the marker concentrations to determine a marker concentration between two different stages, to determine the change in concentration at different stages of gestation to determine the risk of a chromosomal abnormality, since the same marker will eventually be chosen.

8. Davies also does not specifically disclose measuring two biological parameters at two points in time, but just a single value measured at two stages. Nicholls discloses a method for screening for Down's syndrome, where screening levels are measured. Nicholls discloses and teaches that the method involves the steps of first assaying a sample obtained from a pregnant woman at a first stage of pregnancy for at least one biochemical screening marker and measuring at least one screening marking from an ultrasound scan taken at a first stage of pregnancy and measuring at least one screening marker from a second stage of pregnancy. Next, a sample is obtained at a second stage of pregnancy for at least one biochemical marker and measuring at least one screening marker from an ultrasound also taken at the second stage of pregnancy. The risk of Down's syndrome is then measured using the screening marker levels from

both the first and second stages of pregnancy. Since Nicholls discloses measuring at least one biochemical marker and at least one screening marker, this is interpreted to be more than one, for instance at least two, four if you count the screening markers, at two different stages, in which is used for determining the likelihood of Down's syndrome. It is interpreted by the examiner that there is at least a first and second biochemical screening markers are the biological parameters, where there are two stages of pregnancy where each of these two markers are taken (see abstract, page 2, line 26-page 3, line 22, page 5, line 5-page 6, line 12). Furthermore, Nicholls also discloses and teaches that it is known in the art the risk of Down's Syndrome is determined by a statistical analysis of the screening marker levels based on reference data from existing or future studies (see page 3, lines 15-page 4, line 6). It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Davies to incorporate the sampling of two markers and the analysis techniques of using reference or future studies for determining the risk of Down's Syndrome so that the data can provide and yield a higher detection rate at the same false-positive rate or a lower false-positive rate at the same detection rate.

9. Although Davies discloses only one biomarker measured at two different stages and Nicholls measures two more biomarkers at different stages of pregnancy, it would have been obvious to one having ordinary skill in the art at the time the invention was made to duplication the measurement step and determination of a parameter and to measure more than one biomarker in Davies to verify data compared to other women or to modify Nicholls so that there is an individual value for each marker defining each

marker and basing conclusions on one specific parameter and since the court held that mere duplication of parts has no patentable significance unless a new and unexpected result is produced. *In re Harza*, 274 F.2d 669, 124 USPQ 378 (CCPA 1960). Furthermore, measuring more than one biomarker in a subject would help verify results and to replicate any values that may be questionable creating a more dependable and trusted analysis.

10. While Davies and Nicholls do not explicitly disclose the calculation steps forming vectors in the analysis of the markers obtained at different stages of pregnancy, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the calculation and analysis steps of Davies and Nicholls in order to normalize values of the individual woman and while comparing an individual woman's marker to account for or correct for changes in marker levels dues to gestational age. Forming a feature vector using the data obtained by women, can be used for appropriate reference values or predicted values at particular ages and can be used for the normalization of data, which is old and well known in the art at statistical calculations that can be done without undue experimentation and may be conducted out of routing experimentation.

11. Regarding claims 4, 9, 40 and 41, the reference Davies and Nicholls discloses the claimed invention except for the specific correlation parameter, but it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the correlation coefficient to be greater than 0.6 without undue experimentation in relation to selected markers between the first and second values of

biomarkers since there have already been many markers already identified and values assigned to them and because there are many markers to choose from to create a parameter for determine the risk of a chromosomal abnormality.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTINE T. MUI whose telephone number is (571)270-3243. The examiner can normally be reached on Monday-Thursday 7-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Walter Griffin can be reached on (571) 272-1447. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CTM

/Walter D. Griffin/
Supervisory Patent Examiner, Art Unit 1797